Chapter 2

Consequences of sarcoidosis

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Abstract

Background

Sarcoidosis is a multisystem disorder of unknown cause(s). Less specific disabling symptoms, including fatigue and physical impairments, may have a major influence on the daily activities and the social and professional lives of the patients, resulting in a reduced quality of life.

Considerations

A multidisciplinary approach focusing on somatic and psychosocial aspects is recommended. Patients self-perceived knowledge about the importance of exercise and lifestyle should be improved.

Recommendations

Developing the most appropriate therapeutic approach for sarcoidosis requires careful consideration of the possible impact of fatigue, small fiber neuropathy related symptoms, pain, cognitive functioning, and coping strategies.

Conclusion

Personalized medicine and appropriate communication are beneficial.

Introduction

The clinical expression, natural history, and prognosis of sarcoidosis are highly variable and its course is often unpredictable.[1] Clinical manifestations vary with the organs involved.[1,2] The lungs are affected in approximately 90% of patients with sarcoidosis, and the disease frequently also involves the lymph nodes, skin, and eyes. Remission occurs in more than half of patients within 3 years of diagnosis, and within 10 years in two-thirds, with few or no remaining consequences.[2] Unfortunately, up to one-third of patients have persistent disease, leading to significant impairment of their quality of life (QoL).[3] Interpretation of the severity of the sarcoidosis can be complicated by its heterogeneity. Several major concerns of sarcoidosis patients include symptoms that cannot be explained by granulomatous involvement of a particular organ.[4] Apart from lung-related symptoms (e.g. coughing, breathlessness, and dyspnea on exertion), patients may suffer from a wide range of rather nonspecific disabling symptoms.[2,5] These symptoms, such as fatigue, fever, anorexia, arthralgia, muscle pain, general weakness, muscle weakness, exercise limitation, and cognitive failure, often do not correspond with objective physical evidence of disease.[2,5-9] These issues are often troubling to pulmonologists and other sarcoidologists because they do not relate directly to a physiologic abnormality, are difficult to quantify and hence to monitor, and are challenging to treat.[4]

Symptoms such as fatigue can be nonspecific and difficult to objectify. Moreover, absence of evidence does not mean evidence of absence.[5,7] Sarcoidosis-related complaints, including fatigue, may become chronic and affect patients' QoL even after all other signs of disease activity have disappeared.[7,10,11] Hence, patients consult their physician not only with organ-specific symptoms – directly related to the organ(s) involved – but also with nonspecific health complaints, such as fatigue, cognitive failure, exercise intolerance, and muscle weakness.[12] These impairments in sarcoidosis are disabling, especially when they become chronic.[13,14] Sarcoidosis consists of several overlapping clinical syndromes ('the sarcoidoses'), each with its own specific pathogenesis. A complete evaluation of sarcoidosis could make use of a panel with four disease domains or dimensions: extent of disease, severity, activity and impact.[15-17] Severity of sarcoidosis in each organ is defined as the degree of organ damage sustained from sarcoidosis. The interpretation of the severity of sarcoidosis can be complicated by its heterogeneity. The organ damage can be estimated subjectively by the intensity of symptoms, objectively as a percentage decline from normal capacity (e.g. percentage of the predicted normal value on pulmonary function testing) or by critical location of lesions (e.g. cardiac block). However, pulmonary function test results do not always represent changes in the severity of pulmonary sarcoidosis,[18] which illustrates that the demonstration of sarcoid activity remains an enigma. Assessment of inflammatory activity in sarcoidosis patients without deteriorating lung function or radiological deterioration but with unexplained persistent disabling symptoms is an important and often problematic issue. Historically, evaluation of the various available

tools for the assessment of inflammatory activity has been hampered by the lack of a gold standard.

This section focuses on the impact of the broad range of sarcoidosis-related problems on patients' lives.

Symptoms

In addition to symptoms related to the organs involved, patients may suffer from all kinds of less specific symptoms. These sarcoidosis-related disabling symptoms can significantly reduce a person's quality of life (QoL), especially in chronic sarcoidosis.[19] All these symptoms may have major consequences and impact on the patients' lives and those of their relatives.

Fatigue

Fatigue is the most frequently described and devastating symptom in sarcoidosis, and is globally recognized as a disabling symptom. The reported prevalence varies from 60 to 90% of sarcoidosis patients,[5] and up to 25% of fatigued sarcoidosis patients report extreme fatigue. Physicians generally assess disease severity and progression in sarcoidosis on the basis of clinical tests, such as pulmonary function tests, chest radiographs, and serological tests. However, these objective clinical parameters correlate poorly with the patients' subjective sense of well-being.[8,20] Sarcoidosis patients may suffer from substantial fatigue even in the absence of other symptoms or disease-related abnormalities. For example, fatigue and general weakness may persist even after routine clinical test results have returned to normal.[5] There is a positive association between symptoms of suspected small fiber neuropathy (SFN) and fatigue, as well as between dyspnea and fatigue [13,21,22] So far, no organic substrate has been found for the symptoms of sarcoidosis-associated fatigue.

To date, no appropriate definition of fatigue exists. Fatigue can be seen and measured as a unidimensional or multidimensional concept. The multidimensional concept of fatigue can be divided into at least two categories: physical and mental or passive and active fatigue.[5,10]

Some sarcoidosis patients are debilitated by the symptoms of their disease and are unable to work; others are underemployed and incapable of achieving their full potential due to their health issues.[23] Individuals affected by the disease frequently appear completely healthy, so their symptoms are often not taken seriously by family, friends, employers and healthcare professionals. Consequently, some patients lose their desire and ability to effectively socialize with others, causing relationships and family dynamics to ultimately suffer. These combined factors impact on an individual's economic status, interpersonal relationships and family dynamics, increase their stress levels, and induce depression in patients.

The etiology of this troublesome problem remains elusive and is usually multifactorial. Fatigue can be a consequence of the treatment itself, for instance as a complication of corticosteroid therapy. The diagnosis of sarcoidosis-associated fatigue requires extensive evaluation to identify and treat potentially reversible causes.[5,6] Its etiology may involve granuloma formation and cytokine release. However, despite effective treatment of the sarcoidosis, many patients continue to experience fatigue.[5,24] Comorbidities associated with sarcoidosis, including depression, anxiety, hypothyroidism, and altered sleep patterns, may all contribute to fatigue. [23,25] Despite an exhaustive search for treatable clinical causes of fatigue, most patients' complaints of fatigue are not correlated with clinical parameters of disease activity.[5,24]

Dyspnea

Dyspnea is, by definition, subjective, but a greater value should be given to its quantification by validated scales in the initial evaluation and follow-up of patients with sarcoidosis. The mechanism for dyspnea in sarcoidosis is multifactorial. [12,22,26] Research has found that the degree of dyspnea in sarcoidosis does not correlate with lung function tests.[27] Pulmonary function test results do not always reflect changes in the severity of pulmonary sarcoidosis. Moreover, several studies have reported that neither lung function test results nor chest radiographs correlate with nonspecific health complaints or with QoL.[19,28] In the follow-up, the level of dyspnea often, but not always, changes in the same direction as the forced vital capacity (FVC).[29] Spontaneous resolution of radiographic lesions is more common in asymptomatic patients.[17] The intensity of dyspnea at initial evaluation correlates with the need for long-term treatment.[30]

Small fiber neuropathy and autonomic dysfunction

In 2002, small fiber neuropathy (SFN) was recognized as a symptom of sarcoidosis.[31] Unlike granulomatous large neuron involvement, SFN appears to be a common complication occurring in up to 40%[32] to 60% of patients with sarcoidosis.[33]

SFN is a peripheral nerve disorder that selectively affects thinly myelinated Aδ fibers and unmyelinated C fibers.[34] These fibers are associated with thermal and nociceptive sensations, and pathology of these nerves may lead to a 'painful neuropathy'. However, these nerves also affect the autonomic nervous system, and SFN may also lead to an 'autonomic neuropathy' (see also Table 2.1).[35,36]

Symptoms of SFN are disabling for patients, have a high impact on QoL and are often difficult to treat.[35] Damage to or loss of small *somatic* nerve fibers results in pain, burning or tingling sensations, or numbness, typically affecting the limbs in a distal to proximal gradient. Symptoms can be very severe, are usually worse at night and often affect sleep. People sometimes sleep with their feet uncovered because they cannot bear the touch of the sheets. Walking may be difficult due to severe pain caused by the pressure on the floor. When autonomic fibers are affected, patients may experience

dry eyes, dry mouth, orthostatic dizziness, constipation, bladder incontinence, sexual dysfunction, trouble sweating, or red or white skin discolorations (see also Table 2.1).[34] Involvement of cardiac sympathetic nerves might play a role in the prognosis, as indices of autonomic cardiac dysfunction have been identified as strong predictors of cardiovascular morbidity and mortality.[34]

Since routine nerve conduction tests evaluate only large nerve fiber function, and quantitative techniques for the assessment of small nerve fibers are not routinely applied, the diagnosis of SFN can easily be missed.[35,37] This may lead to frustration for both physician and patient due to the failure to diagnose a neuropathic pain syndrome. There is as yet no gold standard for the diagnosis of SFN. Diagnosis is usually established on the basis of clinical features, in combination with abnormal findings of specialized tests such as the assessment of intra-epidermal nerve fiber density (IENFD) in skin biopsy, temperature sensation tests for sensory fibers, and sudomotor and cardiovagal testing for autonomic fibers.[32,33,38]

The Small Fiber Neuropathy Screening List (SFNSL) was developed in a sarcoidosis population as a first screening tool.[21]

Table 2.1 Symptoms suggestive of small fiber neuropathy

Sensory symptoms	
	Pain[a]
	Paresthesia's
	Sheet intolerance
	Restless legs syndrome[b]
Symptoms of autonomic dysfunction	
	Hyperhidrosis or hyperhidrosis
	Diarrhea or constipation
	Urinary incontinence or urine retention
	Gastroparesis
	Sicca syndrome
	Blurry vision
	Facial flushes
	Orthostatic intolerance
	Sexual dysfunction

[a] Pain in small fiber neuropathy often has a burning, tingling, shooting or prickling character; [b] Restless legs syndrome is a disorder characterized by disagreeable leg sensations that usually occur prior to sleep onset and that cause an almost irresistible urge to move.

Psychological burden

Depressive symptoms

Depressive symptoms in sarcoidosis are at least partly an expression of exhaustion due to the ongoing disease. Depressive symptoms have been found to be negatively associated with and affect patients' fatigue scores.[10] In addition, the relationship between fatigue and depressive symptoms parallels the findings for other chronic

illnesses, such as diabetes, chronic obstructive pulmonary disease, cardiac disease, and rheumatoid arthritis.[39] Moreover, the severity and nature of fatigue moderate anxiety and depressive symptoms in sarcoidosis. Fatigue and autonomic dysfunction are both dominant symptoms and risk factors for depression.[40] The symptoms may share several neurobiological abnormalities, for example an increase in TNF-α.[40] The relationship between depressive symptoms and fatigue may also be based on a cytokine imbalance, initiated by an inflammatory immune response in sarcoidosis.[39,41] The cytokine balance of patients suffering from depression also appears to be disturbed.[42]

Not only fatigue, but also psychological symptoms such as depressive symptoms and anxiety play an important role in sarcoidosis.[15,43-46] They have been reported in 17 to 66% of patients with sarcoidosis. Understanding the nature of the relationships between fatigue, depressive symptoms, and anxiety remains difficult, however. The nature of fatigue moderates the relationships between fatigue and anxiety and between fatigue and depressive symptoms in sarcoidosis. In a study by De Kleijn et al., fatigue was often reported with concurrent depressive symptoms (34–36%) and anxiety (43–46%).[47] About one-third of the patients (31%) reported high-trait anxiety as well as high levels of depressive symptoms at baseline. The study also suggested that the relationship between depressive symptoms and fatigue is bidirectional. Depressive symptoms may indirectly lead to more symptoms, as they are associated with poor self-care (diet, exercise, giving up smoking, and medication regimens) in patients with chronic diseases in general.[39] However, physical symptoms and the resulting functional impairments caused by complications of medical illness are also likely to impose a burden on the patient's life and to provoke depression.[39] Hence, not only fatigue but also depressive symptoms and anxiety should be an integral part of the multidisciplinary management of sarcoidosis patients.

Anxiety and stress

Several studies have shown that the prevalence of anxiety in sarcoidosis patients is 33-36%.[47,48] Studies also showed that anxiety was more common in sarcoidosis patients than in the general population and among healthy persons.[49,50] The percentages for anxiety disorders are obviously lower; for instance 6.3% of sarcoidosis patients have a panic disorder.[51] In any case, anxiety is a major problem in sarcoidosis patients. Since fatigue is one symptom that is known to co-occur with anxiety, it is not surprising that anxiety in general and trait anxiety were found to be related to fatigue.[5,24,47] One study also found that trait anxiety predicted fatigue at follow-up.[47] Trait anxiety refers to the tendency of persons to react with anxiety in new situations. In contrast, state anxiety is defined as anxiety that is elicited in a particular situation and does not last long. In addition to fatigue, one study found that the severity of sarcoidosis symptoms was also related to anxiety.[52] Studies of the relation between anxiety and dyspnea reported inconsistent results.[49,53]

Studies examining stress in sarcoidosis are still very scarce. One study found that the magnitude of stressful life events was higher in sarcoidosis patients than in healthy

controls.[54] Patients also appeared to use inadequate coping strategies with regard to stress.[54] Another study reported a relation between increased life stress and impaired lung function.[55] Finally, one study focusing on perceived stress found it to be high and related to sarcoidosis symptoms.[23] Perceived/experienced stress is caused by interpreting a situation as threatening. This indicates that the same situation may be perceived as stressful by one person and as a challenge by another. Interpreting a situation as threatening may result in several reactions known as fight-flight or freeze. In each of these, the person is scared, but this translates into different behavior: anger and aggressive behavior (fight), anxiety and escaping from the situation (flight), or no reaction at all (freeze). Fight and flight reactions require a physical reaction.

Anxiety consists of physical or hyperarousal symptoms, such as increased heart rate, perspiration, and dizziness, which are inherent to the reaction of the sympathetic nervous system.[56] In addition to a physical component, anxiety also has a cognitive component, that is, a thought (or chain of thoughts) that determines the emotion experienced. If someone is confronted with a situation and has thoughts such as 'I can do this' and 'I want to test whether I can overcome this', the situation is regarded as a challenge, and the above physical symptoms will not occur. If the same situation induces thoughts such as 'I cannot handle this' and 'I must do something, but I have no idea what', the situation is perceived as threatening and the physical symptoms related to anxiety will occur. This relationship between stress and anxiety, and the two components of anxiety (cognitive and physical), might explain the relationships found between symptoms and anxiety/stress.

Another aspect to take into consideration is the duration of stress or anxiety. A brief feeling of stress and anxiety is very common and is considered healthy, as the person will use the above fight or flight reactions to cope with the situation. In this sense a parallel can be drawn with pain and fatigue, which are both healthy responses to a stimulus that may harm the body or demand too much of the body, respectively. It becomes unhealthy when the stress and anxiety become persistent, as this will have negative effects on the immune system. In our modern society, physical reactions are often elicited by thoughts that do not require physical action. Think about (recurrent) negative thoughts, such as 'I am a loser', 'My illness makes me a burden to other people', 'Symptoms will probably become worse', and 'I will soon die from this disease'.

From this perspective, various researchers have justly suggested that sarcoidosis patients may benefit from psychological interventions[47,51] focusing on coping and appraisal, such as stress reduction treatment.[23,55] In each case, the basis for the interventions should be a type of cognitive behavioral therapy (CBT), including so-called third generation CBT like mindfulness-based cognitive therapy, as this type of therapy has proved to be effective in patients with anxiety disorder. Finally, it is important to realize that anxiety (just like depressive symptoms/depression) is known to be one of the factors prolonging chronic fatigue, and that chronic fatigue can be successfully treated with CBT.

Cognitive impairment and memory loss

In addition to organ-specific symptoms and non-specific health complaints such as fatigue and physical impairments, patients also have to deal with side-effects of medical treatment. Patients with sarcoidosis often report everyday cognitive deficits.[6] There is growing interest in cognitive failure research in populations of patients with various chronic diseases.[57,58] Functional cognitive impairment, if present, may lead to increased fatigue and low compliance with medical treatment. Currently, however, no data are available on the extent of cognitive underperformance among sarcoidosis patients. Research in multiple sclerosis patients found that memory complaints were not associated with memory performance, but with fatigue complaints.[58] It is tempting to speculate that this may also be the case in sarcoidosis patients. There is a special interest in sarcoidosis due to the high prevalence of fatigue and everyday cognitive failure, together with the relatively young age of the patients.

Physical impairment

Sarcoidosis obviously imposes a burden on patients' lives (see Figure 2.1).[12,59] Symptoms of fatigue and dyspnea induce exercise limitation, while fatigue also leads to physical inactivity, and the specific sarcoidosis symptoms, or the thought of living with a progressive, incurable condition, create anxiety and mood disturbance, and affect emotional well-being. Although less recognized than exertional dyspnea, lack of energy or exhaustion is a very common and frustrating physical symptom in patients with sarcoidosis. Patients with sarcoidosis (as well as other interstitial lung diseases (ILDs)) often have diminished exercise capacity and reduced muscle strength, as demonstrated by reduced oxygen uptake (measured during a maximal cardiopulmonary exercise test) or a shorter-than-predicted distance covered during a six-minute walking test (6MWD). Monitoring which takes muscle strength and exercise capacity into account has been found to improve the routine monitoring of sarcoidosis.[28,60,61] Like others, Marcellis et al. found exercise intolerance and muscle weakness to be frequent problems in sarcoidosis, both in fatigued and nonfatigued patients.[28]

Exercise intolerance in sarcoidosis is most often multifactorial, involving lung-mechanical, musculoskeletal, and gas exchange abnormalities.[12,28,62-64] Several studies have reported that neither lung function test results nor chest radiographs correlate with these nonspecific health complaints, nor with QoL.[11,23,45-47] Moreover, pulmonary function test results at rest appear to be poor predictors of exercise capacity. Changes in gas exchange upon exercise can be fairly accurately predicted by diffusing capacity of the lung for carbon monoxide (DLCO)%,[65,66] but can be present even with normal DLCO.[67] Fatigue, which as mentioned above is one of the major problems in sarcoidosis, can reduce patients' day-to-day functioning.[5] Consequently, reduced physical activity can induce general deconditioning, which in turn contributes to increased perceived fatigue and a sense of dyspnea, as well as insufficient physical activity.[60,68] Assessment of the presence of physical impairments is recommended, as it provides additional

information about the patient's functional status, disease severity, and progression.[28,60,62-64] Since the patients' ability to handle physical activity is clearly decreased, however, the activities should be adjusted, and rehabilitation programs should be carefully designed.[61,69,70]

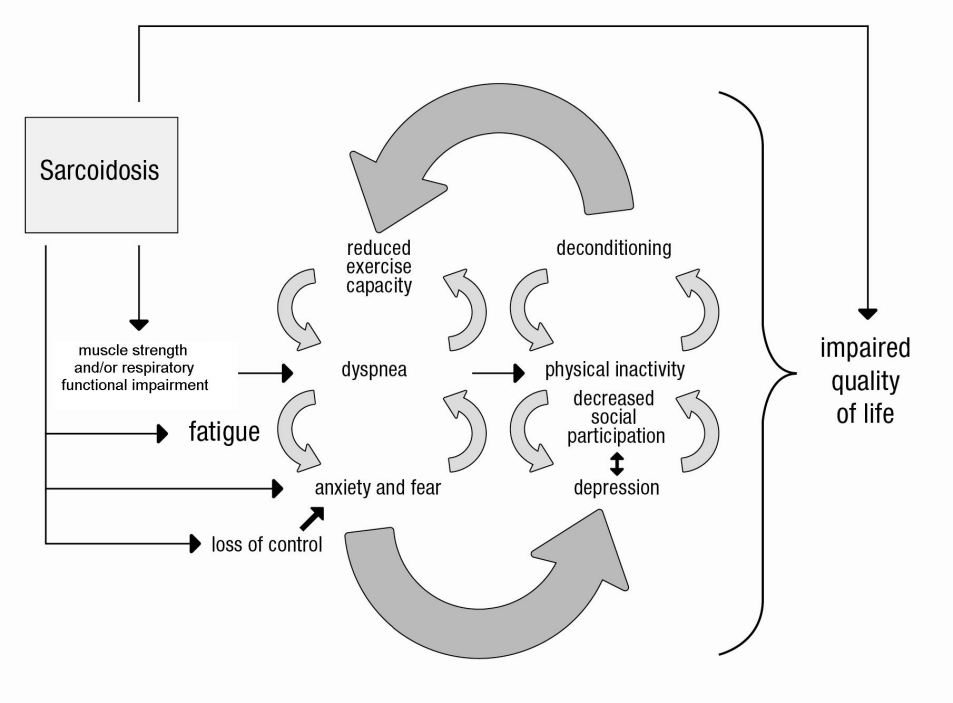

Figure 2.1 Negative vicious circle of physical deconditioning: disabling symptoms in sarcoidosis can reduce daily physical activities, resulting in general deconditioning and a reduced quality of life (adapted from Swigris et al.[59] and previously published[12]).

Overall impact on patients' lives: quality of life

The impact of any disease depends on the way the patient perceives the disease and modifies his/her activities of daily living. Living with a long-term disease like sarcoidosis significantly affects quality of life (QoL), with negative consequences for general health and social and psychosocial well-being.[3,71-73] QoL is an important outcome measure of treatment, especially with regard to chronic diseases. It is a concept that concerns patients' evaluation of their functioning in a wide range of domains, but always including the physical, psychological, and social domains.[3] Assessment covering only these three domains is known as assessment of health-related QoL.[3,73]

QoL is often confused with health status (HS), which concerns patients' physical, psychological, and social functioning.[3] Psychological factors such as burnout, emotional distress, and work-related social support influence levels of QoL.[72] A study among

sarcoidosis patients found that the strongest predictor of all dimensions of QoL was the corresponding QoL at baseline.[13] This might be explained by the fact that sarcoidosis-related symptoms remain relatively stable over time.[13,47] Social support has been described as a buffer against pain and disability, and also as being associated with greater activity levels among individuals with pain.[72,74] Support from friends and family can also be related to the psychological dimensions of QoL.[75] A study among people with chronic pain found that a rich social network was related to higher perceived QoL.[76] Moreover, work-related social support is known to positively predict return to work, while lack of social support at work is a well-known risk factor for development of pain.[77] In sarcoidosis, there is poor agreement between physicians and patients with regard to the perceived symptoms attributable to the disease, with a particular failure of clinicians to recognize the impact of non-organ-specific features.[15,17] It has been proposed that assessment of the health status and QoL of sarcoidosis patients would help bridge this gap, aiding communication and treatment, and complementing existing clinical assessments. Various aspects of sarcoidosis, such as the relatively young age at disease onset, the often unpredictable and chronic nature of the disease, the uncertainly about the cause and the broad range of frequently persistent symptoms may account for the aggravating influence on patients' lives as well as those of their families and friends, especially since a really appropriate treatment of sarcoidosis is still lacking.

Fatigue, breathlessness, reduced exercise capacity, and arthralgia are the most frequently reported symptoms. It appears that these sarcoidosis-related symptoms are associated with a lower QoL.[8,13,44,47,53,78] Women have lower scores on the physical health, psychological health, social relationships, and environmental domains, and the general assessment of overall QoL. Research found that the use of corticosteroids predicted a lower QoL in all domains except spirituality. Having a partner was associated with the QoL domains of psychological health and level of independence, whereas a low educational level predicted better scores for the social relationships domain, while arthralgia predicted poorer scores for this domain.[8] Fatigue had a negative effect on patients' QoL scores for the physical health, psychological health, and level of independence domains.

Treatment options

Pharmacological treatment

There is a lack of standardized management strategies for sarcoidosis. Most sarcoidosis patients show spontaneous resolution of the disease and do not require systemic pharmacological treatment.[2] Glucocorticoids are the cornerstone therapeutic agent, and have a favorable short-term effect on functional impairments, including respiratory impairment and symptoms. However, the long-term beneficial effect remains uncertain. In view of the limitations we are aware of nowadays, authorization would be

doubtful if glucocorticoids were to be introduced at present. A subset of patients will require more aggressive treatment. The published data on the different treatment options in sarcoidosis are limited and the treatment therefore still remains mostly empirical.[2] The decision on whether to start systemic immunosuppressive treatment or not should be based on the patients' symptomatology, including the impact on their QoL, as well as the extent of compromised organ function.

Recent studies have demonstrated the effectiveness of various neurostimulants, including methylphenidate, for the treatment of sarcoidosis-associated fatigue. These and other agents may be useful adjuncts for the treatment of this type of fatigue. There is obviously a need for studies evaluating the causes of, and new therapeutic options for, sarcoidosis-associated fatigue. Psychological interventions should also be examined. Standard sarcoidosis treatments such as those using corticosteroids and other immunosuppressive agents are often ineffective for SFN-related symptoms.[4] Symptomatic neuropathic pain treatment in sarcoidosis patients is not different from the treatment of neuropathic pain from other causes, and consists of antidepressants, anticonvulsants and prolonged-release opioids. However, in common with their effects in other neuropathic pain states, these agents provide limited pain relief in just 30-60% of patients, at the cost of considerable side effects. These data indicate that there is an urgent need for analgesic agents with high efficacy for neuropathic pain patients, causing no debilitating side-effects. Case reports mention beneficial effects of intravenous immunoglobulin and anti-TNF-alpha therapy. [6,79,80] The precise potency of these drugs needs further study however.

Additional alternatives to pharmacological treatment

Developing the most appropriate therapeutic approach for sarcoidosis, including rehabilitation programs, requires careful consideration of the possible impact of pain, the SFN-related symptoms, the fatigue and coping strategies, as well as all other relevant aspects of this multisystemic disease.[3,4,6,49,81] Various treatments are available for fatigue with a partly psychological cause, and patients with a clinical depression can be prescribed antidepressants. Some patients may require help to improve their coping and self-management skills, to improve their QoL. Cognitive therapy may be indicated to treat coping problems or stress perception. Sleeping problems should be treated appropriately.[25] In general, care providers have to raise supportive care issues and provide information about alternative care programs beside medication, which aim to reduce the symptoms and improve the wellbeing of sarcoidosis patients. Patients should be informed about the importance of exercise and they should be encouraged to stay active.

Rehabilitation

Patients should be instructed to lead an as active and involved a life as possible as exercise intolerance and muscle weakness are frequent problems in sarcoidosis influencing QoL (Figure 2.1).[28] Rehabilitation has many benefits for patients with sarcoidosis, including social participation, psychological wellbeing, maintaining levels of activity, learning to use breathing exercises and ways to adapt exercises for the home environment.[69,70,82,83] In the broader context of medical encounters, physical therapy or rehabilitation can help to avoid a negative vicious circle of deconditioning.[61,69] Research has found that fatigue in patients with sarcoidosis was reduced after a period of physical training.[69,70] Moreover, their psychological health and physical functioning also improved.[69] Sarcoidosis patients generally benefit from additional non-pharmacological treatments, not only physical training but also nutritional supplements and counseling.[69,70,84,85] Patients should be counseled about their responsibilities in managing their own condition, about ways to engage different services when required, and about lifestyle, e.g. the importance of regular exercise as well as pulmonary rehabilitation programs. Patients self-perceived knowledge about the importance of exercise for their health (in addition to drug therapy) should be improved. Care providers should be able to refer patients to rehabilitation (including pulmonary rehabilitation) by physical therapists or other professionals with awareness/knowledge of sarcoidosis, if they expect these patients to benefit, or if the patients ask for referral. Rehabilitation services or programs led by physical therapists should be available to patients at reasonable cost. Prospective studies should be designed to answer lingering questions about the value of exercise training for patients with sarcoidosis, including what benefits can be expected of maintenance programs and how long these will last. Our own research found that patients reported less feelings of uncertainty and anxiety after a training program (unpublished data). This has promising implications for clinical practice. As sarcoidosis patients may suffer from various impairments, such as arthralgia, muscle pain, and fatigue, the intensity of the training should be personalized to avoid training aggravating these impairments, resulting in high dropout rates. This also argues for a multidisciplinary approach to the routine management of sarcoidosis.

More research is needed to provide evidence for the relationship between physical therapy and recall. Such studies should assess whether awareness of the importance of physical activities in daily life and their consequences for sarcoidosis patients might affect adherence to treatment or medication regimens. The duration, frequency, and intensity of exercise programs are critical to achieve physical benefits.[82] In general ‘high-frequency, low-impact’ exercise can be recommended. Future prospective studies are warranted to fine-tune the training parameters, duration, and frequency.

Communication and patient participation

Providing information and communication can be hampered by the complexity of sarcoidosis and its heterogeneity. Moreover, management of patients with sarcoidosis requires more than prescribing drugs. It is important for physicians to listen to their patients; it is wise to take what the patient says seriously. Obviously, understanding and remembering medical information is crucial for every patient, as it is a prerequisite for coping with their disease and making informed treatment decisions. Most patients do remember their diagnosis, but have difficulty remembering information about things like treatment plans, recommendations, and side-effects. Patients' information recall may be enhanced by addressing emotions by means of affective communication. Extensive research has shown that physicians' affective communication (i.e., being emotionally supportive; adopting a warm, empathic, and reassuring manner) may improve patients' outcomes, including reduced levels of anxiety and distress.[86,87] Physicians' affective communication not only tempers emotional arousal, but also enhances recall of medical information.[87] Research in various disorders has shown that such affective statements improved recall, especially as regards prognostic information and, to some extent, treatment information. Obviously, since sarcoidosis requires a multidisciplinary approach in view of its wide range of symptoms, communication amongst the various health care workers involved and between them and the patients is of great importance.[88] Although the effect of affective communication has not yet been studied in sarcoidosis, this may be expected to improve patient compliance. Patient participation is increasingly recognized as a key component in the design of health care processes and is also advocated as a means of improving patient compliance. The concept has been successfully applied to various areas of patient care, such as decision making and the management of chronic diseases. Patient participation in shared treatment decision-making is hypothesized to improve treatment adherence and clinical outcomes. Although this has not yet been studied in sarcoidosis, other research findings reveal the significance of patient participation as a key factor in improving treatment adherence and clinical outcome. Quality improvement strategies for sarcoidosis management should therefore emphasize patient participation. Further research is essential to establish key determinants of the success of patient participation in improving efficacy of care for sarcoidosis patients.

Patient participation has promising implications for the multidisciplinary management of sarcoidosis. However, the effect of affective communication on recall should be further established because evidence is lacking, especially for extensive consultations. Other interesting topics for future studies include whether self-perceived medical knowledge about sarcoidosis and its related consequences, including treatment options, is sufficient to achieve beneficial effects.

Summary

Sarcoidosis is a multisystem disorder of unknown cause(s) that imposes a burden on patient's lives. In addition to the specific organ-related symptoms, less specific disabling symptoms, including fatigue and physical impairments, may have a major influence on the daily activities and the social and professional lives of the patients, resulting in a reduced quality of life. A multidisciplinary approach is recommended for these patients, one that focuses on somatic as well as psychosocial aspects of this erratic disorder. Patients self-perceived knowledge about the importance of exercise and lifestyle for their health (in addition to drugs) should be improved. Developing the most appropriate therapeutic approach for sarcoidosis, including rehabilitation programs, requires careful consideration of the possible impact of fatigue, small fiber neuropathy symptoms, pain, cognitive functioning, and coping strategies, as well as all other relevant aspects of this multisystemic disease. Hence, personalized medicine and appropriate communication will be beneficial.

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